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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/561,877	08/02/2006	Michael G. Goggins	61506(71699)	1113

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EXAMINER	
WHISENANT, ETHAN C	

ART UNIT	PAPER NUMBER
1634	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/561,877	GOGGINS ET AL.	
	Examiner	Art Unit	
	Ethan Whisenant	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 December 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4,8-11,13,14 and 17-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) ___ is/are allowed.

6)☒ Claim(s) *1,2,4,8-11,13,14 and 17-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 DEC 05* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

FINAL ACTION

1. The applicant's response (filed 15 DEC 09) to the Office Action has been entered. Following the entry of the claim amendment(s), **Claim(s) 1-2, 4, 8-11, 13-14, 17-24** is/are pending. Rejections and/or objections not reiterated from the previous office action are hereby withdrawn. The following rejections and/or objections are either newly applied or reiterated. They constitute the complete set presently being applied to the instant application.

CLAIM OBJECTIONS

2. **Claim(s) 1 and 8** is /are is objected to for the following minor informality.

Claim 1 is objected to because of the phrase "identity to a the nucleic acid" on line 4. Please clarify.

Claim 8 is objected to because of the phrase " the methylated SPARC nucleic acid molecule comprises has at least" on lines 1-2. Please clarify. Claim 8 also like claim 1 recites the phrase "identity to a the nucleic acid" on lines 2-3.

35 USC § 112 - 1ST PARAGRAPH

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim REJECTIONS under 35 USC § 112- 1ST PARAGRAPH

4. Claim(s) 1-2, 4, 8-11, 13-14, 17-24 is/are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of determining whether a mammalian subject is suffering from or at risk for developing pancreatic cancer which method comprises testing a pancreatic biopsy or pancreatic cell culture or pancreatic juice sample but does not reasonably provide enablement for testing any and all biological sample obtainable from a human subject.

In *In re Wands*, 858 F.2d 731,737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) the court considered the issue of enablement in molecular biology. The Court summarized eight factors to be considered in a determination of "undue experimentation". These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the Claims. The Court also stated that although the level of skill in molecular biology is high, results of experiments in molecular biology are unpredictable.

To begin, the breath of these claims encompass the testing of any biological sample obtainable from a human subject (e.g. blood, plasma, serum, urine, buccal swaps and/or PAP smear, etc.) in order to detect pancreatic cancer and/or detect a subject at risk for developing pancreatic cancer. The applicant presents evidence to support the testing of cultured cells and/or pancreatic biopsy samples/pancreatic juice but fails to show that it is possible to diagnose pancreatic cancer and/or detect a risk for developing pancreatic cancer by analyzing the nucleic acids of blood lymphocytes, for example. While the relative skill in the art is very high (the Ph.D. degree with laboratory experience), it is unpredictable, beyond pancreatic cells, as to what tissues/biological sample can be analyzed in order diagnose pancreatic cancer and/or detect a subject at risk for developing pancreatic cancer. The prior art supports testing biopsies or tumor fragments for specific epigenetic changes (i.e. hyper or hypomethylation of CpG islands in certain specific gene promoters). Furthermore, the prior art (i.e. the applicant's own

work) supports the position that hypermethylation of the promoter region of certain gene and reduced/non-expression of said gene(s) is associated with specific cancers. As regards the quantity of experimentation, every possible tissue sample/ biological sample from numerous individuals, both unaffected individuals and individuals know to have pancreatic cancer, would have been analyzed in order to determine which biological samples, if any, beyond those comprising pancreatic cells can be analyzed to yield the desired result. Accordingly, it is concluded that undue experimentation is required to make the invention as it is claimed. See M.P.E.P. §§ 706.03(n) and 706.03(z).

35 USC § 112- 2nd Paragraph

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

CLAIM REJECTIONS under 35 USC § 112- 2ND PARAGRAPH

6. Claim(s) 1-2, 4, 8-11, 13-14, 17 and 24 is/are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 24 are indefinite as regards the scope of the claimed invention. Claims 1 and 24 recite the phrase "a variant thereof", then recites that the "methylated SPARC nucleic acid molecule comprise at least about 90% sequence identity to the nucleic acid sequence set forth in SEQ ID NO. 1." Does the limitation relate to both SPARC nucleic acid molecule and variants thereof or to only the SPARC nucleic acid molecule. Must the "variant(s)" of the SPARC molecule comprise at least about 90% sequence identity to the nucleic acid sequence set forth in SEQ ID NO. 1? For the evaluation of the prior art the examiner has read this claim as if the variant thererof need not comprise at least about 90% sequence identity to the nucleic acid and thus reads on other genes.

Also it is unclear to the examiner what is intended by the phrase at least about 90% identity or at least about 95% identity. Does a molecule with 85% identity to SEQ ID NO.1 constitute a SPARC nucleic acid molecule? How about one with 50% identity or 25% identity or 10% identity.

Also it is unclear to the examiner what is intended by the phrase "at least about five fold" in Claim 10 and "at least about ten fold" in Claim 11. Does a three fold reduction in expression fall within the scope of the instant invention? How about a three fold reduction in expression? The language used makes the claims ambiguous and thus the scope of the claimed invention cannot be determined.

35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that may form the basis for rejections set forth in this Office action:

> A person shall be entitled to a patent unless --
>
> **(a)** the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> **(b)** the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> **(e)** the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.
> or
> **(e)** the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

CLAIM REJECTIONS UNDER 35 USC § 102

8. **Claim(s) 1, 4, 8, 13-14, 17 and 24** is/are rejected under 35 U.S.C. 102(b) as being anticipated by Schutte et al. [Cancer Research 57 :3126-3130 (1997)].

Claim 1 is drawn to a method for diagnnosing pancreatic cancer which method comprises the detection of a methylated SPARC nucleic acid molecule or a variant thereof in a sample from a subject, wherein the methylated SPARC nucleic acid molecule has at least about 90% sequence identity to a the nucleic acid set forth in SEQ ID NO.: 1.

Schutte et al. teach a method of diagnosing pancreatic cancer which comprises detecting the methylation of CpG residues in the promoter region of the p16 gene (i.e. a variant of the SPARC gene).

Claim 4 is drawn to an embodiment of the method of Claim 1 wherein the sample is obtained from a mammal suspected of having pancreatic cancer.

Schutte et al. teach this limitation.

Claim 8 is drawn to an embodiment of the method of Claim 1 wherein the methylated SPARC nucleic acid molecule has at least about 95% sequence identity to a the nucleic acid set forth in SEQ ID NO.: 1.

For at least the reason(s) recited against Claim 1. Schutte et al. teach a method for diagnosing pancreatic cancer comprising all of the limitations recited in Claim 8.

Claim 13 is drawn to an embodiment of the method of Claim 1 wherein the subject sample is obtained from a mammalian patient. **Claim 14** is drawn to an embodiment of the method of Claim 1 wherein the subject sample is obtained from a human patient. **Claim 17** is drawn to an embodiment of the method of Claim 1 wherein the method of detecting a methylated SPARC nucleic acid comprises methylation specific PCR.

Schutte et al. teach these limitations, See at least pp. 3126-3129 and Figure 1..

Claim 24 is drawn to a method for diagnnosing pancreatic cancer which method comprises the detection of a methylated SPARC nucleic acid molecule or a variant thereof in a sample from a subject, wherein the methylated SPARC nucleic acid molecule has at least about 90% sequence identity to a the nucleic acid set forth in SEQ ID NO.: 1.

Schutte et al. teach a method of diagnosing pancreatic cancer which comprises detecting the methylation of CpG residues in the promoter region of the p16 gene (i.e. a variant of the SPARC gene).

9. Claim(s) 1-2, 4, 8-9, 13-14, 17 and 24 is/are rejected under 35 U.S.C. 102(e) as being anticipated by Goggins [US 2007/0015156] or Goggins et al. [US 2003/0190616].

Claim 1 is drawn to a method for diagnnosing pancreatic cancer which method comprises the detection of a methylated SPARC nucleic acid molecule or a variant thereof in a sample from a subject, wherein the methylated SPARC nucleic acid molecule has at least about 90% sequence identity to a the nucleic acid set forth in SEQ ID NO.: 1.

Goggins teaches a method of diagnosing pancreatic cancer which comprises detecting the methylation status of CpG residues in the promoter region of selected genes (i.e. CLDN5, NPTX2 and/or SARP2) any of which could be called a variant of the SPARC gene.

Claim 2 is drawn to an embodiment of the method of Claim 1 wherein the presence of a methylated SPARC nucleic acid molecule is compared to a sample from a subject without cancer.

Goggins teaches this limitation, see the abstract

Claim 4 is drawn to an embodiment of the method of Claim 1 wherein the sample is obtained from a mammal suspected of having pancreatic cancer.

Goggins teaches this limitation, see at least for example ¶ [0037]

Claim 8 is drawn to an embodiment of the method of Claim 1 wherein the methylated SPARC nucleic acid molecule has at least about 95% sequence identity to a the nucleic acid set forth in SEQ ID NO.: 1.

For at least the reason(s) recited against Claim 1. Goggins teaches a method for diagnosing pancreatic cancer comprising all of the limitations recited in Claim 8.

Claim 9 is drawn is drawn to an embodiment of the method of Claim 1 wherein the nucleic acid molecule is expressed at a lower level in a patient with pancreatic cancer as compared to expression levels in a normal individual.

Goggins teaches this limitation, see at least for example ¶s [0033]- [0034]

Claim 13 is drawn to an embodiment of the method of Claim 1 wherein the subject sample is obtained from a mammalian patient. **Claim 14** is drawn to an embodiment of the method of Claim 1 wherein the subject sample is obtained from a human patient. **Claim 17** is drawn to an embodiment of the method of Claim 1 wherein the method of detecting a methylated SPARC nucleic acid comprises methylation specific PCR.

Goggins teaches teach these limitations, See at least ¶s [0033]- [0034] and Figure 4.

Claim 24 is drawn to a method for diagnnosing pancreatic cancer which method comprises the detection of a methylated SPARC nucleic acid molecule or a variant thereof in a sample from a subject, wherein the methylated SPARC nucleic acid molecule has at least about 90% sequence identity to a the nucleic acid set forth in SEQ ID NO.: 1.

Goggins teaches a method of diagnosing pancreatic cancer which comprises detecting the methylation status of CpG residues in the promoter region of selected genes (i.e. CLDN5, NPTX2 and/or SARP2) any of which could be called a variant of the SPARC gene.

35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> **(a)** A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligations under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

CLAIM REJECTIONS UNDER 35 USC § 103

12. **Claim(s) 2, 9-11** is/are rejected under 35 U.S.C. 103(a) as being unpatentable over Schutte et al. [Cancer Research 57 :3126-3130 (1997)] as applied against Claim 1 above and further in view of Shuber [US 2003/0087258(2003)].

Claim 2 is drawn to an embodiment of the method of Claim 1 wherein the presence of a methylated SPARC nucleic acid molecule is compared to a sample from a subject without cancer.

Schutte et al. as argued above teach a method for diagnosing pancreatic cancer comprising all of the limitations of Claim 2 except these authors do not teach comparing the methylation pattern obtained from a subject (i.e. person suspected of having

pancreatic cancer) to sample from a subject without cancer. Schutte teach analyzing "normal tissue i.e. cancer free tissue samples from the cancer patients In addition, Schutte et al. teach analyzing the methylation pattern of the p16 promoter region of HeLa cells but fail to teach analyzing sample(s) from a subject without cancer. However, Shuber teach a method diagnosing CRC by investigating the methylation status of certain genes wherein the methylation status of said genes in cancer biopsy sample is compared to the methylation status of said genes in individuals without cancer (i.e. negative controls), see for example paragraph [0009]. Therefore, absent an unexpected result it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the method of Schutte et al. wherein instead of normal tissue from the patient being tested for cancer the negative control comprises a sample taken from an individual without cancer. Please note that substitution of one well known method/reagent with known properties for a second well known method/reagent with well known properties would have been *prima facie* obvious to the ordinary artisan at the time of the invention in the absence of an unexpected result. As regards the motivation to make the substitution recited above, the motivation to combine arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making this obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

Claim 9 is drawn is drawn to an embodiment of the method of Claim 1 wherein the nucleic acid molecule is expressed at a lower level in a patient with pancreatic cancer as compared to expression levels in a normal individual.

Based on the data presented in Schutte et al. and Shuber, it would have been expected that the expression of the p16 gene would be at a lower level in a patient with pancreatic cancer as compared to expression levels in a normal individual. In support of this position note the expression studies shown in Figure 2 of Schutte et al.

Claim 10 is drawn is drawn to an embodiment of the method of Claim 1 wherein the nucleic acid molecule is expressed at least about five fold lower level in a patient with pancreatic cancer as compared to expression levels in a normal individual.

Claim 11 is drawn is drawn to an embodiment of the method of Claim 1 wherein the nucleic acid molecule is expressed at least about ten fold lower level in a patient with pancreatic cancer as compared to expression levels in a normal individual.

Schutte et al. teach these limitations, see Figure 2.

RESPONSE TO APPLICANT'S AMENDMENT/ ARGUMENTS

13. Applicant's arguments with respect to the claimed invention have been fully and carefully considered but are moot in view of the new ground(s) of rejection.

CONCLUSION

14. Claim(s) 1-2, 4, 8-11, 13-14 and 18-24 is/are rejected and/or objected to for the reason(s) set forth above.

15. Applicant's amendment necessitated the new grounds of rejection. Accordingly, **THIS ACTION IS MADE FINAL.** See M.P.E.P. § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ethan Whisenant whose telephone number is (571) 272-0754. The examiner can normally be reached Monday-Friday from 8:30 am -5:30 pm EST or any time via voice mail. If repeated attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen, can be reached at (571) 272-0731.

The Central Fax number for the USPTO is (571) 273-8300. Please note that the faxing of papers must conform with the Notice to Comply published in the Official Gazette, 1096 OG 30 (November 15, 1989).

/Ethan Whisenant/
Primary Examiner
Art Unit 1634